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8/27/04

TOWNSEND and TOWNSEND and CREW LLP

By:

Juditha Co. Sam

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Heidrun Engler et al.

Application No.: 10/055,863

Filed: January 22, 2002

For: COMPOSITIONS AND METHODS
FOR ENHANCING DELIVERY OF
THERAPEUTIC AGENTS TO CELLS

Examiner: Wilson

Art Unit: 1632

INFORMATION DISCLOSURE
STATEMENT UNDER 37 CFR §1.97 and
§1.98

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Sir:

The references cited on attached form PTO/SB/08A and PTO/SB/08B are being called to the attention of the Examiner. In accordance with 37 CFR §1.98(d), copies of the references can be found in Application No. 08/584,077, filed 01/08/1996 (Pat. No. 5,789,244, issued 08/04/1998, Attorney Docket No. 016930-000800US), Application No. 08/889,355, filed 07/08/1997 (Attorney Docket No. 016930-000811US) and Application No. 09/112,074, filed 07/08/1998 (Pat. No. 6,392,069, issued 05/21/2002, Attorney Docket No. 016930-000812US).

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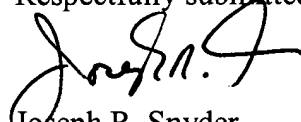
It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

This IDS is being filed before the mailing date of the final Office Action or Notice of Allowance.

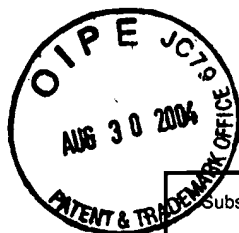
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Respectfully submitted,



Joseph R. Snyder
Reg. No. 39,381

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 925-472-5000
Fax: 925-472-8895
JS:mrv



Substitute for form 1449A/PTO			Complete if Known	
			Application Number	10/055,863
INFORMATION DISCLOSURE STATEMENT BY APPLICANT			Filing Date	January 22, 2002
			First Named Inventor	Engler, Heidrun
			Art Unit	1632
			Examiner Name	Wilson
(use as many sheets as necessary)			Attorney Docket Number	016930-000816US
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U.S. PATENT DOCUMENTS+					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number Kind Code ² (if known)			
	1	5,013,556 A	05-07-1991	Woodle et al.	
	2	5,108,921 A	04-28-1992	Low et al.	
	3	5,166,320 A	11-24-1992	Wu et al.	
	4	5,213,804 A	05-25-1993	Martin et al.	
	5	5,279,833 A	01-18-1994	Rose	
	6	5,283,185 A	02-01-1994	Epand et al.	
	7	5,334,761 A	08-02-1994	Gebeyehu et al.	
	8	5,346,701 A	09-13-1994	Heiber et al.	
	9	5,521,291 A	05-28-1996	Curjel et al.	
	10	5,542,935 A	08-06-1996	Unger et al.	
	11	5,552,309 A	09-03-1996	March	
	12	5,554,386 A	09-10-1996	Groman et al.	
	13	5,578,475 A	11-26-1996	Jessee	
	14	5,580,859 A	12-03-1996	Felgner et al.	
	15	5,589,466 A	12-31-1996	Felgner et al.	
	16	5,601,818 A	02-11-1997	Freeman et al.	
	17	5,631,236 A	05-20-1997	Woo et al.	
	18	5,804,566 A	09-08-1998	Carson et al.	
	19	6,210,939 B1	04-03-2001	Gregory et al.	

FOREIGN PATENT DOCUMENTS								
Examiner Initials*	Cite No. ¹	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³	Number ⁴	Kind Code ⁵ (if known)				
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	24	WO	94/06922		03-31-1994			<input type="checkbox"/>
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	26	WO	95/11984		05-04-1995			<input type="checkbox"/>
	27	WO	97/05209		02-13-1997			<input type="checkbox"/>
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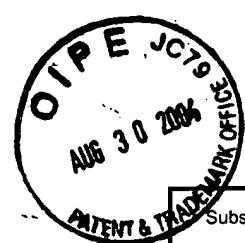
Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known	
				Application Number	10/055,863
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				First Named Inventor	Engler, Heidrun
				Art Unit	1632
				Examiner Name	Wilson
Sheet	2	of	5	Attorney Docket Number	016930-000816US

NON PATENT LITERATURE DOCUMENTS			
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	29	Abe, A. et al., "Transduction of a drug-sensitive toxic gene into human leukemia cell lines with a novel retroviral vector" PSEBM 203:354-359 (1993)	
	30	Arteaga, C. et al., "Tissue-targeted antisense c-fos retroviral vector inhibits established breast cancer xenografts in nude mice" Cancer Research 56:1098-1103 (1996)	
	31	Aungst, B. and Rogers, N., "Comparison of the effects of various transmucosal absorption promoters on buccal insulin delivery" Inter. J. Pharmac. 53:227-235 (1989)	
	32	Banerjee, A. et al., "Changes in growth and tumorigenicity following reconstitution of retinoblastoma gene function in various human cancer cell types of microcell transfer of chromosome 13" Cancer Research 52:6297-6304 (1992)	
	33	Bass, C. et al., "Recombinant adenovirus-mediated gene transfer to genitourinary epithelium in vitro and in vivo" Cancer Gene Ther. 2(2):97-104 (1995)	
	34	Blixt, Y. et al., "Enhancement of intracellular uncoating of adenovirus in HeLa cells in the presence of benzyl alcohol as a membrane fluidizer" Arch. Virol. 129:265-277 (1993)	
	35	Boulikas, "Gene therapy of prostate cancer: p53, suicidal genes, and other targets" Anticancer Research 17:1471-1506 (1997)	
	36	Brewster, S. et al., "Gene therapy in urological oncology: principles, strategies and potential" Eur. Urol. 25:177-182 (1994)	
	37	Cairns, P. et al., "Loss of heterozygosity at the RB locus is frequent & correlates with muscle invasion in bladder carcinoma" Oncogene 6:2305-2309 (1991)	
	38	Cancer Facts & Figures 1995, Am. Canc. Soc. 5-11 (1995)	
	39	Cooper, M. et al., "Safety-modified episomal vectors for human gene therapy" PNAS USA 94:6450-6455	
	40	Curiel, D. et al., "Adenovirus enhancement of transferring-polylysine-mediated gene delivery" PNAS USA 88:8850-8854 (1991)	
	41	Dalesandro, J. et al., "Cardiac and pulmonary replacement" J. Thoracic Cardio. Surg. 111(2):416-422 (1996)	
	42	Fujimoto, K. et al., "Frequent association of p53 gene mutation in invasive bladder cancer" Cancer Research 52:1393-1398 (1992)	
	43	Ginsberg, H. et al. "Role of early region 3 (E3) in pathogenesis of adenovirus disease" PNAS USA 86:3823-3827 (1989)	
	44	Good, N. et al., "Hydrogen ion buffers for biological research" Biochemistry 5(20):467-477 (1966)	

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STATEMENT BY APPLICANT**

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Sheet **3** of **5****Complete if Known**

Application Number	10/055,863
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First Named Inventor	Engler, Heidrun
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Examiner Name	Wilson
Attorney Docket Number	016930-000816US

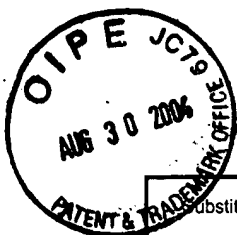
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	45	Goodrich, D. et al., "Expression of the retinoblastoma gene product in bladder carcinoma cells associates with a low frequency of tumor formation" Cancer Research 52:1968-1973 (1992)	
	46	Greenberg, R. et al., "Intravesical AD32 (N-trifluoroacetyladiamycin-14-valerate) in the treatment of patients with refractory bladder carcinoma- clinical efficacy, pharmacology and safety" Proc. Am. Urol. Assoc. 153(supp 233a):19 (1995)	
	47	Grenay, H. et al., "Characterization of imidazoline binding protein(s) solubilized from human brainstem: studies with [³ H] idazoxan and [³ H]clonidine" Neurochem. Int. 25(2):183-191 (1994)	
	48	Helenius et al., "Properties of Detergents" In: Methods in Enzymology, Vol. 56, 734-749 (1979)	
	49	Hemstrom, C. et al., "Gene product of region E4 of adenovirus type 5 modulates accumulation of certain viral polypeptides" J. Virol. 62(9):3258-3264 (1988)	
	50	Huang, S. et al., "A cellular protein that competes with SV40T antigen for binding to the retinoblastoma gene product" Nature 350:160-162 (1991)	
	51	Janout, V. et al., "Evidence for highly cooperative binding between molecular umbrella-spermine conjugates and DNA" Bioconjugate Chem. 8:891-895 (1997)	
	52	Janout, V. et al., "Molecular umbrellas" J. Am. Chem. Chem. Soc. 118:1573-1574 (1996)	
	53	Ji, W. et al., "Inhibition of hepatitis B virus by retroviral vectors expressing antisense RNA" J. Viral. Hep. 4:167-173 (1997)	
	54	Kaneda, Y. et al., "Prevention of restenosis by gene therapy" Annals N.Y. Acad. Sci. 811:299-310 (1997)	
	55	Koc, O. et al., "Transfer of drug resistance genes into hemotopoietic progenitors to improve chemotherapy tolerance" Sem. Oncol. 23(1):46-64 (1996)	
	56	Langer et al., "Biocompatible controlled release polymers for delivery of polypeptides and growth factors" J. Cell Biochem. 45:340-345 (1991)	
	57	Lee, R. et al., "Lipidic vector systems for gene transfer" Crit. Rev. Ther. Drug Carrier Sys. 14(2):173-206 (1997)	
	58	Li, Q. et al., "Assessment of recombinant adenoviral vectors for hepatic gene therapy" Hum. Gene. Ther. 4:403-409 (1993)	
	59	Makarov, S. et al., "Suppression of experimental arthritis by gene transfer of interleukin 1 receptor antagonist cDNA" PNAS USA 93:402-406 (1996)	
	60	Marshall, E., "Gene therapy's growing pains" Science 269:1050-1055 (1995)	

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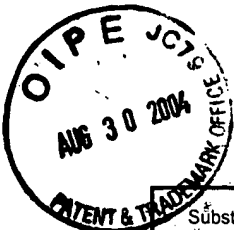
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Sheet	4	of	5		

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	61	Miller, N. et al., "Targeted vectors for gene therapy" FASEB J. 9:190-199 (1995)	
	62	Monson, F. et al., "Indigocarmine as a quantitative indicator of urothelial integrity" J. Urol. 145:842-845 (1991)	
	63	Morris, B. et al., "Adenoviral-mediated gene transfer to bladder in vivo" J. Urol. 152:506-509 (1994)	
	64	Murayama, Y. et al., "Antisense oligonucleotides to p53 tumor suppressor suppress the induction of apoptosis by epidermal growth factor in NCI-H 596 human lung cancer cells" Antisense Nucl. Acid Drug Devel. 7:109-114 (1997)	
	65	Niidome, T. et al., "Binding of cationic α -helical peptides to plasmid DNA and their gene transfer abilities into cells" J. Biol. Chem. 272(24):15307-15312 (1997)	
	66	Nolta, J. et al., "Transduction of pluripotent human hematopoietic stem cells demonstrated by clonal analysis after engraftment in immune-deficient mice" PNAS USA 93:2414-2419 (1996)	
	67	Parsons, C. et al., "Bladder surface glycosaminoglycans: an epithelial permeability barrier" J. Urol. 143:139-142 (1990)	
	68	Pinnaduwaage, P. et al., "Use of a quaternary ammonium detergent in liposome mediated DNA transfection of mouse L-cells" Biochim. Biophys. Acta 985:33-37 (1989)	
	69	Plank, C. et al., "The influence of endosome-disruptive peptides on gene transfer using synthetic virus-like gene transfer systems" J. Biol. Chem. 269(17):12918-12924 (1994)	
	70	Raper, S. et al., "Safety and feasibility of liver-directed ex vivo gene therapy for homozygous familial hypercholesterolemia" Annals Surgery 223(2):116-126 (1996)	
	71	Rosenberg, S. "The immunotherapy and gene therapy of cancer" J. Clin. Oncol. 10(2):180-199 (1992)	
	72	Ross et al., "Gene therapy in the United States: a five-year status report" Human Gene Therapy 7:1781-1790 (1996)	
	73	Sandberg, J. et al., "Improving access to intestinal stem cells as a step toward intestinal gene transfer" Human Gene Therapy 5:323-329 (1994)	
	74	Shawaphun et al., "Chemical evidence for transbilayer movement of molecular umbrellas" J. Am. Chem. Soc. 121:5860-5864 (1999)	
	75	Spandidos, D. et al., "Expression of the normal H-ras gene can suppress the transformed and tumorigenic phenotypes induced by mutant ras genes" Anticancer Research 10:1543-1554 (1990)	
	76	Takahashi, R. et al., "The retinoblastoma gene functions as a growth and tumor suppressor in human bladder carcinoma cells" PNAS USA 88:5257-5261 (1991)	

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	77	Verma et al., "Gene therapy- promises, problems and prospects" Nature 389:239-242 (1997)	
	78	Vidal, P. et al., "Nouvelle stratégie pour vectorisation d-ARN dan des cellules de mammifères. Utilisation d'un vecteur peptidique" CR Acad. Sci. III 32:279-287 (1997)	
	79	Wills, K. et al., "Development and characterization of recombinant adenoviruses encoding human p53 for gene therapy of cancer" Hum. Gene Ther. 5:1079-1088 (1994)	
	80	Wills, K. et al., "Gene therapy for hepatocellular carcinoma: Chemosensitivity conferred by adenovirs- mediated transfer of the HSV-1 thymidine kinase gene" Cancer Gene Ther. 2(3):191-197 (1995)	
	81	Wu, G. et al., "Receptor-mediated gene delivery and expression in vivo" J. Biol. Chem. 263(29):14621-14624 (1988)	
	82	Xiao, X. et al., "Adeno-associated virus (AAV) vector antisense gene transfer in vivo decreases GABA _A σ ₁ containing receptors and increases inferior collicular seizure sensitivity" Brain Res. 756:76- 83 (1997)	
	83	Yew, N. et al., "Optimization of plasmid vectors for high-level expression in lung epithelial cells" Human Gene THerapy 8:575-584 (1997)	

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